Claims

1. Preparations for the application, administration or transport of at least one active ingredient, especially for medicinal or biological purposes, into and through barriers and constrictions, such as skin or the like, in the form of liquid droplets, which can be suspended in a liquid medium and are provided with a membrane-like sheath of one or a few layers of amphiphilic carrier substance, the carrier substance comprising at least two physicochemically different components, characterized in that at least two components are provided, which differ in their solubility in the suspension medium of the preparations, usually water, by a factor of at least 10 and in that the content of solubilizing components is less than 0.1 mole percent, based on the content of these substances, at which the solubilization point of the enveloped droplets is reached or this solubilization point cannot be reached.

2. The preparation of claim 1, characterized in that the amphiphilic components are selected so that, independent of concentration, there is no solubilization.

3. The preparation of claims 1 and 2, characterized in that the solubility, especially the water solubility of the more soluble component(s) is/are at least 10^{-3} to 10^{-6} M and the solubility, especially the water solubility, of the less soluble component(s) is/are at least 10^{-6} to 10^{-10} M.

4. The preparation of one of the claims 1 to 3, characterized in that the difference between the solubility of the more soluble component(s) and the less soluble component(s) is approximately between 10 and 10^7, preferably between 10^2 and 10^6 and especially between 10^3 and 10^5.

5. The preparation of one of the claims 1 to 4, characterized in that the ability of the preparation to permeate through constrictions is at least 0.001% and preferably 0.1% of the permeability of small molecules, which permeate essentially without being impeded.

6. The preparation of one of the claims 1 to 5, characterized in that the ratio of the permeation capability relative to reference particles $P_{(transfer.)}/P_{(refer.)}$, the reference particles being, for example water, much smaller than the constrictions in the barrier, when the barrier itself is the site of the determination, is between 10^{-5} and 1, preferably between 10^{-4} and 1 and especially between 10^{-2} and 1.

7. The preparation of one of the claims 1 to 6, characterized in that the preparations contain at least two amphiphilic components of different solubility, for forming a carrier substance and/or a membrane-like sheath about a droplet amount of hydrophilic liquid, wherein the active ingredient is contained in the carrier substance in or at the membrane-like sheath and/or in the hydrophilic liquid.

8. The preparation of one of the claims 1 to 7, characterized in that the vesicle radius of the

enveloped droplets is between about 25 and about 500 nm, preferably between about 50 and about 200 nm and especially between 80 and about 100 nm.

9. The preparation of one of the claims 1 to 8, characterized in that the sheath is a double layer.

10. The preparation of one of the claims 1 to 9, characterized in that the amphiphilic component (n) comprises or comprise physiologically tolerated lipids of different polarity and/or such an active ingredient or ingredients.

11. The preparation of one of the claims 1 to 10, characterized in that the amphiphilic substance comprises a lipid or lipoid of biological origin or a corresponding synthetic lipid or a derivative of such lipids, particularly diacyl or dialkyl glycerophosphoethanolamino azo polyoxyethylene derivative, didecanoyl phosphatidyl choline, diacyl phosphooligomaltobionamide, a glyceride, a glycerophospholipid, isoprenoid lipid, sphingolipid, steroid, sterol, a sulfur-containing or hydrocarbon-containing lipid or a different lipid, which forms stable structures, such as double layers, preferably comprises a half protonated liquid fatty acid, particularly a phosphatidyl choline, phosphatidyl ethanolamine, phosphatidyl glycerol, phosphatidyl inositol, a phosphatid acid, a phosphatidyl serine, a sphingomylein or sphingophospholipid, glycosphingolipid (such as cerebroside, ceramide polyhexoside, sulfatide, sphingoplasmalogen), ganglioside or other glycolipid, or a synthetic lipid, preferably a dioleoyl, dilinolyl, dilinolenyl, dilinoloyl, dilinolinoyl or diarachinoyl, dilauroyl, dimyristoyl, dilalmitoyl, distearoyl phospholipid or a corresponding dialkyl or sphingosin derivative, glycolipid or other identical chain or mixed chain acyl lipid or alkyl lipid.

12. The preparation of one of the claims 1 to 11, characterized in that the less soluble amphiphilic component comprises a synthetic lipid, preferably myristoleoyl, palmitoleoyl, petroselinyl, petroselaidyl, oleoyl, elaidyl, cis- or trans-

vaccenoyl, linolyl, linolenyl, linolaidyl, octadecatetraenoyl, gondoyl, eicosaenoyl, eicosadienoyl, eicosatrienoyl, arachidoyl, cis- or trans-docosaenoyl, docosadienoyl, docosatrienoyl, docosatetraenoyl, caproyl, lauroyl, tridecanoyl, myristoyl, pentadecanoyl, palmitoyl, heptadecanoyl, stearoyl or nonadecanoyl, glycero-phospholipid or a corresponding chain-branched derivative or a corresponding sphingosin derivative, glycolipid or a different acyl lipid or alkyl lipid; and the more soluble component or components is derived from one of the less soluble components listed above and, for increasing the solubility, is derivatized with a butanoyl, pentanoyl, hexanoyl, heptanoyl, octanoyl, nonanoyl, decanoyl, dodecane or undecanoyl or a corresponding monounsaturated or polyunsaturated or chain-branched substituent thereof or several substituents, selected independently of one another, and/or is substituted, complexed and/or associated with a different material, which is suitable for improving the solubility.

13. The preparation of one of the claims 1 to 12, characterized in that the total content of amphiphilic substance for administration on human or animal skin is between 0.01 and 40% by weight of the preparation, preferably between 0.1 and 15% by weight and especially between 1 and 10% by weight.

14. The preparation of one of the claims 1 to 13, characterized in that the total content of amphiphilic substance for application on plants is 0.000001 to 10% by weight, preferably between 0.001 and 1% by weight and especially between 0.01 and 0.1% by weight.

15. The preparation of one of the claims 1 to 14, characterized in that, as active ingredient, it contains an adrenocorticostatic agent, a β-adrenolytic agent, an androgen or antiandrogen, an anti-parasitic, anabolic, anesthetic or analgesic, analeptic, anti-allergic, anti-arrhythmic, anti-arteriosclerosis, anti-asthmatic and/or bronchospasmolytic agent, an antibiotic, an anti-depressive and/or anti-psychotic agent, an anti-diabetic agent, an antidote, an anti-emetic, anti-epileptic, anti-

fibrinolytic, anti-convulsive or anti-cholinergic agent, an enzyme, coenzyme or a corresponding inhibitor, an antihistamine, an antihypertensive drug, a biological activity inhibitor, an antihypotensive agent, an anticoagulant, an anti-mycotic or antimyasthenic agent, an active ingredient against Parkinson's or Alzheimer's disease, an anti-phlogistic, anti-pyretic or anti-rheumatic agent, an antiseptic, a respiratory analeptic or stimulating agent, a broncholytic, cardiotonic or chemotherapeutic agent, a coronary dilator, a cytostatic agent, a diuretic, a ganglion blocker, a glucorcorticoid, a therapeutic agent for influenza, a hemostatic or hyptonic agent, immunoglobulin or fragment or a different immunological or receptor substance, a bioactive carbohydrate (derivative), a contraceptive, a migraine agent, a mineral corticoid, a morphine antagonist, a muscle relaxant, a narcotic, a neural or CNS therapeutic agent, a nucleotide or polynucleotide, a neuroleptic agent, a neuron transmitter or a corresponding antogonist, a peptide (derivative), an ophthalmic agent, a (para)-sympathicomimetic or (para)-sympathicolytic agent, a protein (derivative), a psoriasis/neurodermatitis agent, a mydriatic agent, a mood elevator, rhinological agent, a sleeping draft or its antagonist, a sedative, a spasmolytic, tuberculosis or urological agent, a vasoconstrictor or dilator, a virostatic agent or a wound-healing agent or several such agents, especially diclofenac or ibuprofen.

16. The preparation of one of the claims 1 to 15, characterized in that the active ingredient is a nonsteroidal anti-inflammatory drug, for example, diclofenac, ibuprofen or a lithium, sodium, potassium, cesium, rubidium, ammonium, monoethyl, dimethyl, trimethylammonium or ethylammonium salt thereof.

17. The preparation of one of the claims 1 to 16, characterized in that the less polar component comprises a physiologically compatible lipid, preferably from the class of phospholipids and especially from the class of phosphatidyl cholines, and the active ingredient is the more soluble component, optionally with the addition of less than 10% by weight, based on the total composition of the preparation, of a further soluble component, which is the more soluble component,

the concentration of the more soluble component(s) typically being between 0.01% by weight and 15% by weight, preferably between 0.1% by weight and 10% by weight and particularly between 0.5% by weight and 3% by weight, and the total lipid concentration being between 0.005% by weight and 40% by weight and preferably between 0.5% by weight and 15% by weight and especially between 1% by weight and 10% by weight.

18. The preparation of one of the claims 1 to 17, characterized in that the preparation comprises consistency modifiers, such as hydrogels, antioxidants such as probucol, tocopherol, BHT, ascorbic acid, desferroxamine and/or stabilizers such as phenol, cresol, benzyl alcohol, etc.

19. The preparation of one of the claims 1 to 18, characterized in that the active ingredient is a growth regulating substance for living beings.

20. The preparation of one of the claims 1 to 18, characterized in that the active ingredient has biocidal properties and, in particular, is an insecticide, pesticide, herbicide or fungicide.

21. The preparation of one of the claims 1 to 18, characterized in that the active ingredient is an allurement, in particular, a pheromone.

22. A method for producing a preparation for the administration, application or transport of at least one active ingredient, particularly for medicinal or biological purposes, into and through natural barriers and constrictions, such as skin and the like, in the form of liquid droplets, which can be suspended in a liquid medium and are provided with a membrane-like sheath of one or a few layers of amphiphilic carrier substance, the carrier substance comprising at least two physicochemically different components, characterized in that at least two amphiphilic components are selected, which differ in their solubility in the suspension

medium of the preparation, usually water, by a factor of at least 10 and the content of solubilizing components is less than 0.1 mole percent, based on the content of these substances, at which the solubilizing point of the enveloped droplets is reached or this point cannot be reached in a practically relevant region, and the content of amphiphilic components is adjusted, so that the ability of the preparation to permeate through constructions is at least 0.001% of the permeability of small molecules, for example, of water.

23. The method of claim 22, characterized in that the content of amphiphilic components is adjusted, so that the ratio of the permeation capability relative to reference particles, which are much smaller than the constrictions in the barrier, for example water, when the barrier itself is the site of determination, is between 10^{-5} and 1, preferably between 10^{-4} and 1 and especially between 10^{-2} and 1.

24. The method of claims 22 and 23, characterized in that stability and permeation capability are determined by filtration, optionally under pressure, through a fine-pored filter or through otherwise controlled mechanical whirling up, shearing or comminuting.

25. The method of one of the claims 22 to 24, characterized in that the substance mixture for producing a transfersome-like preparation is subjected to a filtration, to a treatment with ultrasound, to stirring, to shaking or to other mechanical comminuting effects.

26. The method of one of the claims 22 to 25, characterized in that transfersome-like droplets, which form the preparation, are produced from at least two amphiphilic components of different polarity, at least one polar liquid and at least one active ingredient.

27. The method of one of the claims 22 to 26, characterized in that the transfersome-like droplets, which form the preparation, wherein the amphiphilic component(s) comprises or contains the active ingredient, are formed from at least two amphiphilic components of different polarity and at least one polar liquid.

28. The method of one of the claims 22 to 28, characterized in that the amphiphilic components and the hydrophilic substance in each case are mixed separately with the active ingredient and optionally brought into solution, the mixtures or solutions are then combined into a mixture, in which droplet formation is brought about by supplying, in particular, mechanical energy.

29. The method of one of the claims 22 to 28, characterized in that the amphiphilic components, either as such or dissolved in a physiologically compatible solvent or dissolving intermediary, which is miscible with a polar liquid or liquids, especially with water, are combined with a polar solution.

30. The method of one of the claims 22 to 29, characterized in that the formation of enveloped droplets is brought about by stirring, by evaporation from a reverse phase, by an injection method or a dialysis method, by electrical, thermal or mechanical stressing, such as shaking, stirring, homogenizing, ultrasonicating, rubbing, freezing or thawing, heating or cooling or high pressure or low pressure filtration.

31. The method of one of the claims 22 to 30, characterized in that the formation of the enveloped droplets is brought about by filtration and the filter material has a pore size of 0.01 to 0.8 μm, especially of 0.05 to 0.3 μm and particularly of 0.08 to 0.15 μm, several filters optionally being connected in series.

32. The method of one of the claims 22 to 31, characterized in that the association between carrier and active ingredients takes place at least partially after the droplet formation.

33. The method of one of the claims 22 to 32, characterized in that, shortly before use, the enveloped droplets are prepared from a concentrate or lyophilisate.

add A5 add C1 add 74